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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/620,061

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EXAMINER

KUBELIK, ANNE R

ART UNIT

PAPER NUMBER

1638

MAIL DATE

DELIVERY MODE

05/01/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/620,061

Applicant(s)

BLUMWALD ET AL.

Examiner

Anne R. Kubelik

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 February 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-23 and 26-33 is/are rejected.
- 7) ☒ Claim(s) 24 and 25 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

1. Claims 21-33 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. While applicant has amended the priority claim in the first paragraph of the specification, the priority claims in the application data sheet and the Declaration still claim priority to 60/395,670. The Declaration is thus objected to.
4. The objection to claims 2-19 and 21-22 because of informalities is withdrawn in light of Applicant's cancellation or amendment of the claims.
5. The rejection of claims 1-9, 11-12 and 20-21 under 35 U.S.C. 102(e) as being anticipated by Gaxiola (US 2002/0023282 A1, filed August 2000) is withdrawn in light of Applicant's amendment of the claims.
6. The rejection of claims 1-9, 11-12 and 14-17 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Young et al (WO 91/06651) is withdrawn in light of Applicant's amendment of the claims.
7. The rejection of claim 22 under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Gaxiola (US 2002/0023282 A1, filed August 2000) is withdrawn in light of Applicant's amendment of the claims.
8. The rejection of claims 18-19 under 35 U.S.C. 103(a) as being unpatentable over Young et al (WO 91/06651) is withdrawn in light of Applicant's amendment of the claims.

Art Unit: 1638

9. The rejection of claims 1-20 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21 of copending Application No. 10/617,623 is withdrawn in light of the abandonment of that application.

10. The rejections of claims 1-20 the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 3 and 5-34 of U.S. Patent No. 6,936,750 and claims 1-20 of U.S. Patent No. 7,041,875 is withdrawn in light of Applicant's cancellation of the claims.

11. The provisional rejections of claims 1-20 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 9-11 and 18-21 of copending Application No. 10/617,624, claims 17 and 19-48 of copending Application No. 11/067,456, claims 17 and 19-48 of copending Application No. 11/067,558, claim 17 and 19-48 of copending Application No. 11/065,977, and claims 1-13 and 19-20 of copending Application No. 10/520,497 is withdrawn in light of Applicant's cancellation of the claims.

Claim Objections

12. Claims 23-24 are objected to because of the following informalities:

In claim 23, line 3, and claim 24, line 2, there is an improper article before "nucleic".

13. Claims 24-25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, and, for claim 24, to address the objection above.

Claim Rejections - 35 USC § 112

14. Claims 21-23 and 26-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 8 September 2006, as applied to claims 1-22. Applicant's arguments filed 2 February 2007 have been fully considered but they are not persuasive.

A full review of the specification indicates that plants transformed with nucleic acids encoding Na^+/H^+ transporters are essential to the operation of the claimed invention. The claims, however, are drawn to any non-naturally occurring non-halophyte plant that accumulates sodium in its vacuoles; this encompasses mutant plants, plants transformed with nucleic acids encoding proteins other than Na^+/H^+ transporters, as well as plants transformed with nucleic acids encoding Na^+/H^+ transporters.

The specification describes the structures of some Na^+/H^+ transporters, but the structures that make them vacuolar Na^+/H^+ transporters are not described. The specification fails to describe nucleic acids encoding proteins other than Na^+/H^+ transporters that result in sodium accumulation in vacuoles and fails to describe any mutant plants.

The specification fails to describe nucleic acids that hybridize to SEQ ID NO:1 under the conditions recited in claim 14, and fails to recite a function for those nucleic acids.

One of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species.

Art Unit: 1638

Hence, Applicant has not, in fact, described non-naturally occurring non-halophyte plants within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the claimed compositions, it is not clear that Applicant was in possession of the claimed genus at the time this application was filed.

Applicant urges that the claims have been amended to recite a method for lowering the soil salt content by cultivating a plants comprising a recombinant construct encoding a vacuolar Na^+/H^+ transporter (response pg 7).

This is not found persuasive because the recombinant construct encoding a vacuolar Na^+/H^+ transporter has not been described within the full scope of the claims.

15. Claims 21-23 and 26-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for plants transformed with a nucleic acid encoding SEQ ID NO:1, does not reasonably provide enablement for any non-naturally occurring non-halophyte plant that accumulates sodium in its vacuoles. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Due to Applicant's amendment of the claims, the rejection is modified from the rejection set forth in the Office action mailed 8 September 2006, as applied to claims 1-22. Applicant's arguments filed 2 February 2007 have been fully considered but they are not persuasive.

Art Unit: 1638

The claims are broadly drawn to a method of lowering the salt content of soil by growing a plant transformed with nucleic acids that encode vacuolar Na^+/H^+ transporters, including those that hybridize to SEQ ID NO:1.

The instant specification, however, only provides guidance for analysis of the Na^+ , K^+ , sugars, proline, protein, and nitrogen content in various plant parts of AtNHX1 (SEQ ID NO:2) transformed *Brassica napus*; plants grown in high salt had an increase in Na^+ and proline and a decrease in K^+ and sugars in leaves and roots (example 1); analysis of H^+ -dependent Na^+ and K^+ movement and ion, sugar and proline contents of high-salt grown AtNHX1 (SEQ ID NO:2) transformed tomato (example 2); prophetic expression of AtNHX1 in yeast (example 3).

The instant specification fails to provide guidance for the full scope of nucleic acids that encode vacuolar Na^+/H^+ transporters, including those that hybridize to SEQ ID NO:1.

The instant specification fails to provide guidance for which amino acids of SEQ ID NO:2 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain vacuolar Na^+/H^+ transporter activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

Making substitutions in proteins does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the “conservative” substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while “nonconservative” substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are

Art Unit: 1638

substituted with the “nonconservative” amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the “conservative” amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins, however, would have at least 95% identity to the original protein. The nucleic acids encoding all these mutated proteins, however, would hybridize under high stringency to the nucleic acids encoding the original protein.

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids that hybridize to SEQ ID NO:1. Making all possible single amino acid substitutions in an 538 amino acid long protein like that encoded by SEQ ID NO:1 would require making and analyzing 19^{538} nucleic acids; these proteins would have 99.8% identity to SEQ ID NO:2. Because nucleic acids that hybridize to SEQ ID NO:1 would encode proteins with many amino acid substitutions, many more than 19^{538} nucleic acids would need to be made and analyzed.

Guo et al (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Thus, making and analyzing proteins with many amino acid substitutions that also have vacuolar Na^+/H^+ transporter activity would require undue experimentation.

As the specification does not non-naturally occurring non-halophyte plants within the full scope of the claims, undue trial and error experimentation would be required to screen through the myriad of plants, to identify those with sodium accumulation in their vacuoles, if such plants are even obtainable.

Art Unit: 1638

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

Applicant urges that enablement only requires that the specification teach one of skill in the art how to make and use the invention - methods for growing and harvesting transgenic plants are well-known in the art, guidance is given for methods of making transgenic plants, and method for identifying vacuolar Na^+/H^+ transporters other than those in Table III and SEQ ID NO:2 (response pg 8).

This is not found persuasive. The rejection is not that methods for growing and harvesting plants are not enabled or that general methods for making transgenic plants are not enabled. The rejection is that nucleic acids that encode vacuolar Na^+/H^+ transporters, including those that hybridize to SEQ ID NO:1 are not enabled. The proteins in Table III are NXH gene products (§31), which, the closest definition in the specification, is a gene product that when ectopically expressed increases salt tolerance (§53). The specification does not identify the proteins in the specification as vacuolar Na^+/H^+ transporters. Further, it is not clear that nucleic acid encoding any of these would hybridize to SEQ ID NO:1 under the conditions recited in claims 23 or 26-27.

Applicant urges that it is the nature, not the amount, of experimentation required that matters; testing if a particular nucleic acid is a vacuolar Na^+/H^+ transporter merely requires testing the activity by methods known in the art and testing for salt accumulation in plant parts as described in examples 1 and 2 (response pg).

Art Unit: 1638

This is not found persuasive because methods of assays do not teach how to make the claimed nucleic acids.

16. Claims 23, 25 and 29-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Due to Applicant's amendment of the claims, the rejection is different from the rejection set forth in the Office action mailed 8 September 2006, as applied to claims 1-22. Applicant's arguments filed 2 February 2007 have been fully considered but they do not apply to these new rejections.

Claim 23 lacks antecedent basis for the limitation "the nucleotide sequence of (a)" in part (b).

Claim 25 is definite in its recitation of "the same amino acid sequence as encoded by the nucleotide sequence of SEQ ID NO:1", as any given nucleotide sequence can encode multiple proteins as it has 6 reading frames. It is suggested that Applicant replace the phrase with --SEQ ID NO:2--, if that is what was intended. Claim 23, part (b) is similarly indefinite.

Claim 29 lacks antecedent basis for the limitation "the 35S promoter".

Claim 30 lacks antecedent basis for the limitation "the CaMV promoter".

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

Art Unit: 1638

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

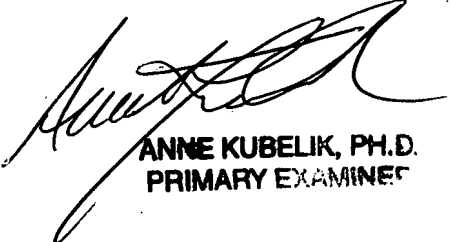
The central fax number for official correspondence is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Anne Kubelik, Ph.D.
April 25, 2007



ANNE KUBELIK, PH.D.
PRIMARY EXAMINER